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## CLAIMS

[Claim(s)]

[Claim 1]

It is the antigen joint protein containing a complex of the first two polypeptide and the second two polypeptide,

the first polypeptide has an antigen binding site located in an amino terminal of an immunoglobulin light chain regular domain ( $C_L$  domain) -- here -- this  $C_L$  domain -- the

[ immunoglobulin heavy chain ] -- stably combinable with a 1 regular domain ( $C_H1$  domain) --

and

The second polypeptide has an antigen binding site located in an amino terminal of this  $C_H1$  domain, and 1 which can perform stable self-bonding, or a heavy chain regular domain beyond it is behind this  $C_H1$  domain,

Antigen joint protein.

[Claim 2]

The antigen joint protein according to claim 1 in which 1 or said antigen binding site beyond it is provided by the single strand Fv.

[Claim 3]

The antigen joint protein according to claim 1 which has the singularity from which said antigen binding site of said first and the second polypeptide differs.

[Claim 4]

The antigen joint protein according to claim 1 which has the singularity with said same antigen binding site of said first and the second polypeptide.

[Claim 5]

The antigen joint protein according to claim 3 which is a thing to an epitope which exists on an antigen in which said singularity differs.

## [Claim 6]

The antigen joint protein according to claim 3 which is a thing to an epitope which exists on the antigen with said same singularity.

## [Claim 7]

The antigen joint protein according to claim 1 in which said first polypeptide and the second polypeptide are carrying out the covalent bond.

## [Claim 8]

The antigen joint protein according to claim 1 in which said second two polypeptide is carrying out the covalent bond.

## [Claim 9]

The antigen joint protein according to claim 1 in which said second polypeptide has  $C_H1$  of an antibody of isotype IgA, IgD, or IgG,  $C_H2$ , and  $C_H3$  domain.

## [Claim 10]

The antigen joint protein according to claim 1 in which said second polypeptide has  $C_H1$  of an antibody of isotype IgE or IgM,  $C_H2$ ,  $C_H3$ , and  $C_H4$  domain.

## [Claim 11]

The antigen joint protein according to claim 1 in which said regular domain is a regular domain of mammalian.

## [Claim 12]

The antigen joint protein according to claim 1 in which said regular domain is a Homo sapiens regular domain.

## [Claim 13]

The antigen joint protein according to claim 1 in which 1 or said single strand Fv beyond it is the mouse single strand Fv.

## [Claim 14]

The antigen joint protein according to claim 1 which is the chimera single strand Fv in which 1 or said single strand Fv beyond it has the Homo sapiens framework region.

## [Claim 15]

The antigen joint protein according to claim 1 in which said single strands Fv are Homo sapiens  $V_L$  and  $V_H$  domain.

## [Claim 16]

The antigen joint protein according to claim 1 chosen from a group to which said heavy chain regular domain where stable self-bonding can be performed changes from  $C_H2$  of the arbitrary immunoglobulin isotypes or the subtype origins,  $C_H3$ , and  $C_H4$  domain.

## [Claim 17]

The antigen joint protein according to claim 1 combinable with an Fc receptor.

[Claim 18]

The antigen joint protein according to claim 1 which can take effect a complement agency cell damage (CMC).

[Claim 19]

The antigen joint protein according to claim 1 which can take effect an antibody dependency cell agency cell damage (ADCC).

[Claim 20]

The antigen joint protein according to claim 1 connected with an antitumor agent.

[Claim 21]

The antigen joint protein according to claim 1 connected with detectable quality of signal output.

[Claim 22]

The antigen joint protein according to claim 1 which neutralizes activation of a VEGF receptor.

[Claim 23]

The antigen joint protein according to claim 22 whose VEGF receptor is a thing of mammalian.

[Claim 24]

The antigen joint protein according to claim 22 whose VEGF receptor belongs to human being.

[Claim 25]

The antigen joint protein according to claim 24 in which the code of the VEGF receptor is carried out by flt-1 or flk-1 gene.

[Claim 26]

It is the antigen joint protein according to claim 1 with at least one piece specific to KDR among said antigen binding sites.

[Claim 27]

It is the antigen joint protein according to claim 1 with at least one piece specific to FLT1 among said antigen binding sites.

[Claim 28]

It is the antigen joint protein according to claim 1 with at least one piece specific to FLT4 among said antigen binding sites.

[Claim 29]

It is the antigen joint protein according to claim 1 with at least one piece specific to EGF-R among said antigen binding sites.

[Claim 30]

It is the antigen joint protein according to claim 1 with at least one piece specific to HER2 among said antigen binding sites.

## [Claim 31]

It is the antigen joint protein according to claim 1 with at least one piece specific to FGF-R among said antigen binding sites.

## [Claim 32]

It is the antigen joint protein according to claim 1 with at least one piece specific to PDGF-R among said antigen binding sites.

## [Claim 33]

It is the antigen joint protein according to claim 1 with at least one piece specific to receptor tyrosine kinase among said antigen binding sites.

## [Claim 34]

It is the antigen joint protein according to claim 1 with at least one piece specific to Tek among antigen binding sites.

## [Claim 35]

It is the antigen joint protein according to claim 1 with at least one piece specific to Tie-2 among said antigen binding sites.

## [Claim 36]

The antigen joint protein according to claim 1 with one side specific to KDR among said antigen binding sites, and said binding site of another side specific to FLT1.

## [Claim 37]

The antigen joint protein according to claim 1 with one side specific to KDR among said antigen binding sites, and an antigen binding site of another side specific to an antigen chosen from a group which comprises FLT4, EGF-R, HER2, FGF-R, PDGF-R, Tek, and Tie2.

## [Claim 38]

The antigen joint protein according to claim 1 with one side specific to EGF-R among said antigen binding sites, and an antigen binding site of another side specific to HER2.

## [Claim 39]

It is the antigen joint protein according to claim 1 with at least one piece specific to a cell surface antigen of an immune system effector cell among said antigen binding sites.

## [Claim 40]

The antigen joint protein according to claim 39 whose immune system effector cell is a T cell, a macrophage, neutrophil leucocyte, or a spontaneous killer cell.

## [Claim 41]

The antigen joint protein according to claim 39 in which said cell surface antigen is CD3, CD16, CD28, CD32, CD64, an Fc receptor, a cytokine receptor, or a lymphokine receptor.

## [Claim 42]

The antigen joint protein according to claim 39 in which said cell surface antigen is a receptor of cytokine or lymphokine, and an antigen binding site includes cytokine, lymphokine, or some

[ those ] amino acid sequences.

[Claim 43]

The antigen joint protein according to claim 42 whose receptor is a receptor of IL-2, IL-4, IL-5, GM-CSF, or G-CSF.

[Claim 44]

Antigen joint protein given in any 1 paragraph of claims 26, 27, 28, 29, 30, 31, 32, 33, 34, and 35 with one piece specific to a cell surface antigen of an immune system effector cell in which said antigen binding site strikes.

[Claim 45]

The antigen joint protein according to claim 44 in which said immune system effector cell is a T cell, a macrophage, neutrophil leucocyte, or a spontaneous killer cell.

[Claim 46]

The antigen joint protein according to claim 44 in which said cell surface antigen is CD3, CD16, CD28, CD32, CD64, an Fc receptor, a cytokine receptor, or a lymphokine receptor.

[Claim 47]

It is the antigen joint protein containing a complex of the first two polypeptide and the second two polypeptide,

the first polypeptide has the single strand Fv located in an amino terminal of an immunoglobulin light chain regular domain ( $C_L$  domain) -- here -- this  $C_L$  domain -- the

[ immunoglobulin heavy chain ] -- stably combinable with a 1 regular domain ( $C_H1$  domain) -- and

The second polypeptide has the single strand Fv located in an amino terminal of this  $C_H1$  domain, and 1 which can perform stable self-bonding, or a heavy chain regular domain beyond it is behind this  $C_H1$  domain here,

Antigen joint protein.

[Claim 48]

The antigen joint protein according to claim 47 which has the singularity from which an antigen binding site of said first and the second polypeptide differs.

[Claim 49]

The antigen joint protein according to claim 47 which has the singularity with same antigen binding site of said first and the second polypeptide.

[Claim 50]

The antigen joint protein according to claim 47 which neutralizes activation of KDR.

[Claim 51]

The antigen joint protein according to claim 50 in which both said both [ one side or ] Fv are single strand Fv p1c11.

## [Claim 52]

The antigen joint protein according to claim 50 in which both said both [ one side or ] Fv are single strand Fv p4G7.

## [Claim 53]

The antigen joint protein according to claim 47 which neutralizes activation of FLT1.

## [Claim 54]

The antigen joint protein according to claim 53 in which both said both [ one side or ] Fv are single strand Fv 6.12.

## [Claim 55]

An amino acid sequence of a complementarity determining region (CDR) of one side of said single strand Fv or both,

At CDRH1, it is the array number 1.;

At CDRH2, it is the array number 2.;

At CDRH3, it is the array number 3.;

At CDRL1, it is the array number 4.;

CDRL2 -- array number 5; -- and

At CDRL3, it is the array number 6,

The antigen joint protein according to claim 50 come out of and shown.

## [Claim 56]

A nucleotide sequence which encodes a complementarity determining region (CDR) of one side of said single strand Fv or both,

About CDRH1, it is the array number 9.;

About CDRH2, it is the array number 10.;

About CDRH3, it is the array number 11.;

About CDRL1, it is the array number 12.;

CDRL2 -- array number 13; -- and

About CDRL3, it is the array number 14,

The antigen joint protein according to claim 50 come out of and shown.

## [Claim 57]

An amino acid sequence of a variable domain of one side of said single strand Fv or both, a heavy chain variable domain ( $V_H$ ) -- array number 7; -- and

About a light chain variable domain ( $V_L$ ), it is the array number 8,

The antigen joint protein according to claim 50 come out of and shown.

## [Claim 58]

A nucleotide sequence which encodes a variable domain of one side of said single strand Fv or both,

a heavy chain variable domain ( $V_H$ ) -- array number 15; -- and

About a light chain variable domain ( $V_L$ ), it is the array number 16,

The antigen joint protein according to claim 50 come out of and shown.

[Claim 59]

An amino acid sequence of a complementarity determining region (CDR) of one side of the single strand Fv or both,

At CDRH1, it is the array number 1.;

At CDRH2, it is the array number 21.;

At CDRH3, it is the array number 3.;

At CDRL1, it is the array number 4.;

CDRL2 -- array number 5; -- and

At CDRL3, it is the array number 6,

The antigen joint protein according to claim 50 come out of and shown.

[Claim 60]

A nucleotide sequence which encodes a complementarity determining region (CDR) of one side of said single strand Fv or both,

About CDRH1, it is the array number 9.;

About CDRH2, it is the array number 24.;

About CDRH3, it is the array number 11.;

About CDRL1, it is the array number 12.;

CDRL2 -- array number 13; -- and

About CDRL3, it is the array number 14,

The antigen joint protein according to claim 50 come out of and shown.

[Claim 61]

An amino acid sequence of a variable domain of one side of said single strand Fv or both, a heavy chain variable domain ( $V_H$ ) -- array number 22; -- and

About a light chain variable domain ( $V_L$ ), it is the array number 23,

The antigen joint protein according to claim 50 come out of and shown.

[Claim 62]

A nucleotide sequence which encodes a variable domain of one side of said single strand Fv or both,

a heavy chain variable domain ( $V_H$ ) -- array number 25; -- and

About a light chain variable domain ( $V_L$ ), it is the array number 26,

The antigen joint protein according to claim 50 come out of and shown.

[Claim 63]

The antigen joint protein according to claim 50 in which both said both [ one side or ] Fv have a



nucleotide sequence shown with the array number 27 or the array number 28.

[Claim 64]

(a) In a host cell,

A recombinant DNA assembly thing which encodes the first polypeptide that has an antigen binding site located in an amino terminal of an immunoglobulin light chain regular domain ( $C_L$  domain), here -- this  $C_L$  domain -- the [ immunoglobulin heavy chain ] -- stably combinable with a 1 regular domain ( $C_H1$  domain) -- and

Behind this  $C_H1$  domain, 1 which can perform stable self-bonding, or a heavy chain regular domain beyond it is a recombinant DNA assembly thing which encodes the second polypeptide that has an antigen binding site located in an amino terminal of this  $C_H1$  domain, and here,

carrying out a simultaneous manifestation by sufficient time and a method to carry out a manifestation of this polypeptide, and formation of this antigen joint protein --; -- and

(b) Collect these antigen joint proteins,

How to manufacture antigen joint protein containing things.

[Claim 65]

A method according to claim 64 which has said assembly thing on the same DNA expression vector.

[Claim 66]

A method according to claim 64 on a DNA expression vector from which said assembly thing differs.

[Claim 67]

A way according to claim 64 said host cell is a bacterial cell, a yeast cell, or a mammalian cell.

[Claim 68]

A method according to claim 64 by which said antigen joint protein is secreted from a host cell.

[Claim 69]

How to neutralize activation of a VEGF receptor including processing a cell in the antigen joint protein of sufficient quantity to neutralize activation of said this receptor according to claim 1.

[Claim 70]

It is the method according to claim 69 that at least one piece is specific to KDR, among said antigen binding sites.

[Claim 71]

It is the method according to claim 69 that at least one piece is specific to FLT1, among said antigen binding sites.

[Claim 72]

How to reduce growth of a tumor with at least one piece specific to a VEGF receptor among said antigen binding sites here including processing a cell in the antigen joint protein of sufficient quantity to reduce growth of a tumor according to claim 1.

[Claim 73]

It is the method according to claim 72 that at least one piece is specific to KDR, among said antigen binding sites.

[Claim 74]

It is the method according to claim 72 that at least one piece is specific to FLT1, among said antigen binding sites.

[Claim 75]

How to check vascularization with at least one piece specific to a VEGF receptor among antigen binding sites here including processing a cell in the antigen joint protein of sufficient quantity to check vascularization according to claim 1.

[Claim 76]

It is the method according to claim 75 that at least one piece is specific to KDR, among said antigen binding sites.

[Claim 77]

It is the method according to claim 75 that at least one piece is specific to FLT1, among said antigen binding sites.

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[Translation done.]

## Drawing selection Drawing 1

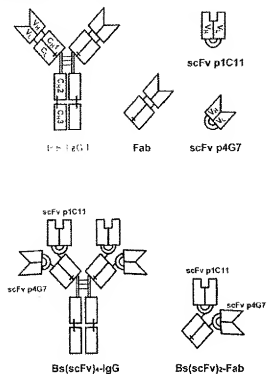


FIG. 1

[Translation done.]